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     (FILE 'HOME' ENTERED AT 11:13:29 ON 09 FEB 2000)

     FILE 'CAPLUS' ENTERED AT 11:13:33 ON 09 FEB 2000

     FILE 'REGISTRY' ENTERED AT 11:13:42 ON 09 FEB 2000
L1            12 S "GLUTAMIC ACID DECARBOXYLASE"

     FILE 'CAPLUS' ENTERED AT 11:15:14 ON 09 FEB 2000
L2             0 S (157092-25-6/RN) AND (PARKINSONS(W)DISEASE)
L3             1 S (157092-25-6/RN)
L4          2004 S "GLUTAMIC ACID DECARBOXYLASE"
L5            28 S L4 AND (PARKINSON?)
L6             0 S L5 AND (ANTISENSE OR RIBOZYME OR TRIPLEX OR AS-ODN OR
OLIGONU
L7             1 S L5 AND (RETICULATA)
               S 9024-58-2/REG#

     FILE 'REGISTRY' ENTERED AT 11:19:57 ON 09 FEB 2000
L8             1 S 9024-58-2/RN

     FILE 'CAPLUS' ENTERED AT 11:19:57 ON 09 FEB 2000
L9          3138 S L8
L10           38 S L9 AND PARKINSON?
L11            3 S L10 AND RETICULATA
L12           48 S L9 AND (GAD(W)65)
L13            0 S L12 AND PARKINSON?
L14            0 S L12 AND RETICULATA
L15            1 S L12 AND (ANTISENSE OR TRIPLEX OR RIBOZYME)
L16           31 S L9 AND (GAD(W)67)
L17            1 S L16 AND (ANTISENSE OR TRIPLEX OR RIBOZYME OR APTAMER)
L18            0 S L16 AND PARKINSONS
L19            0 S L16 AND PARKINSON?
L20            0 S L16 AND PARKIN?
L21            7 S L16 AND DISEASE
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L21 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:774829 CAPLUS
DOCUMENT NUMBER: 130:123530
TITLE: Transcription of a broad range of self-antigens in human thymus suggests a role for central mechanisms in tolerance toward peripheral antigens
AUTHOR(S): Sospedra, Mireia; Ferrer-Francesch, Xavier; Dominguez, Orlando; Juan, Manuel; Foz-Sala, Marius; Pujol-Borrell, Ricardo
CORPORATE SOURCE: Dep. Cell Biol., Physiol., Immunol., Faculty Medicine, Autonomous Univ. Barcelona, Barcelona, 08193, Spain
SOURCE: J. Immunol. (1998), 161(11), 5918-5929
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of the thymus in the induction of tolerance to peripheral antigens is not yet well defined. One impending question involves how the thymus can acquire the diversity of peripheral non-thymic self-Ags for the process of neg. selection. To investigate whether peripheral Ags are synthesized in the thymus itself, the authors have detd. the expression of a panel of circulating and cell-bound peripheral Ags, some of which are targets of autoimmune **diseases**, at the mRNA level in total thymic tissue and in its main cellular fractions. Normalized and calibrated RT-PCR expts. demonstrated the presence of transcripts of non-thymic self-Ags in human thymi from 8 days to 13-yr-old donors. Out of 12 glands, albumin transcripts were found in 12; insulin, glucagon, thyroid peroxidase, and glutamic acid decarboxylase (**GAD**)-**67** in six, thyroglobulin in five, myelin basic protein and retinal S Ag in three, and GAD-65 in one. The levels of peripheral Ag transcripts detected were age-related but also showed marked inter-individual differences. Cytokeratin-pos. stromal epithelial cells, which are a likely cellular source for these, contained up to 200 transcript copies of the most expressed peripheral Ags per cell. These results implicate the human thymus in the expression of wide representation of peripheral self-Ags and support the view that the thymus is involved in the establishment of tolerance to peripheral Ags. The existence of such central mechanism of tolerance is crucial for the understanding of organ-specific autoimmune **diseases**.

L21 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:772026 CAPLUS
DOCUMENT NUMBER: 128:46794
TITLE: Differences in the retinal GABA system among control, spastic mutant and retinal degeneration mutant mice
AUTHOR(S): Yazulla, Stephen; Studholme, Keith M.; Pinto, Lawrence H.
CORPORATE SOURCE: Department of Neurobiology and Behavior, University at

[redacted]Stony Brook, Stony Brook, NY, [redacted]794-5230, USA
SOURCE: Vision Res. (1997), 37(24), 34[redacted]3482
CODEN: VISRAM; ISSN: 0042-6989
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immunocytochem. methods were used to compare the GABA system in control mice and two mutant strains: spastic which has reduced glycine receptors and retinal degeneration mutant in which the photoreceptors degenerate and reportedly have increased GABA and GAD levels. We found that the spastic mutant retina had reduced GABA-immunoreactivity (IR) in the proximal retina, reduced staining for GAD-1440 in the OPL, and reduced GABAA receptor staining in the OPL, compared to control. The retinal degeneration mutant retinas had enhanced GABA-IR throughout the retina, particularly in Muller cells, bipolar cells and IPL, and enhancement of GABAA receptor staining in the OPL, compared to control. The distributions of GABA-IR, GAD-1440-IR and GABAA receptor-IR in retinas of spastic mutant mice that also expressed the retinal degeneration phenotype resembled those found in retinas of mice that expressed only the retinal degeneration phenotype rather than those that expressed only the spastic mutation. No differences were obsd. among the conditions for GAD-65, **GAD-67** or GABA-T. Our results with the spastic and retinal degeneration mutant mice demonstrate that attenuation in the glycinergic system and photoreceptor degeneration, resp., is accompanied by alterations in different aspects of the GABA system, giving impetus for caution in the interpretation of expts. involving genetic manipulation of complex phenotypes.

L21 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:45007 CAPLUS
DOCUMENT NUMBER: 124:84724
TITLE: Glutamic acid decarboxylase autoantibodies in stiff-man syndrome and insulin-dependent diabetes mellitus exhibit similarities and differences in epitope recognition
AUTHOR(S): Daw, Kendra; Ujihara, Noriko; Atkinson, Mark; Powers, Alvin C.
CORPORATE SOURCE: Div. Endocrinol., Vanderbilt Univ., Nashville, TN, 37232, USA
SOURCE: J. Immunol. (1996), 156(2), 818-25
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glutamic acid decarboxylase (GAD) is an autoantigen in two autoimmune **diseases**, insulin-dependent diabetes mellitus (IDDM) and stiff-man syndrome (SMS). However, most individuals with one of these **diseases** do not have the other **disease**. Prior studies have suggested that the natures of the GAD Abs assocd. with each of these **diseases** are different, which may have implications for the autoimmune pathogenesis. The authors compared the GAD autoantibody profile and have mapped GAD protein epitope regions in the two **diseases** using an immunopptn. assay with recombinant GAD 65 and **GAD 67** proteins, GAD protein fragments, and synthetic GAD peptides, as well as chimeric GAD proteins. The results indicate that individuals with SMS have GAD Abs in 100-500-fold higher titer than individuals with IDDM. The population of GAD Abs in SMS sera is quite complex and includes those that recognize at least three GAD 65 epitope regions located between amino acids 1-16, 188-442, and 442-563. These types of GAD Abs are not found in IDDM sera. All SMS sera also had Ab specificity that binds **GAD 67** in a region highly homologous to amino acids 188-442 of GAD 65. In contrast to prior studies

that used immunob[redacted]ting to measure GAD Abs, the a[redacted]ors find GAD Abs in SMS sera also target two conformation-dependent re[redacted]ns of GAD 65, one located in the middle and one near the C-terminus of the protein. These two regions of the GAD 65 protein are similar to regions targeted by GAD 65-specific Abs found in individuals with IDDM. Thus, although **disease**-specific epitopes may exist, there is also overlap in the humoral response between the two **diseases**.

L21 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:729257 CAPLUS
DOCUMENT NUMBER: 123:196405
TITLE: Prevention of autoimmune diabetes in nonobese diabetic female mice by treatment with recombinant glutamic acid decarboxylase (GAD 65)
AUTHOR(S): Pleau, Jean-Marie; Fernandez-Saravia, Flavia; Esling, Anne; Homo-Delarche, Francoise; Dardenne, Mireille
CORPORATE SOURCE: Hopital Necker, Universite Rene Descartes, Paris V, Paris, 75015, Fr.
SOURCE: Clin. Immunol. Immunopathol. (1995), Volume Date 1995, 76(1 Pt. 1), 90-5
CODEN: CLIIAT; ISSN: 0090-1229
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nonobese diabetic (NOD) mouse spontaneously develops insulin-dependent diabetes (IDDM or type I diabetes), resulting from T-lymphocyte-mediated destruction of pancreatic .beta. cells. This autoimmune phenomenon includes mononuclear cell infiltration of the islets of Langerhans (insulitis) and the presence of circulating autoantibodies. The specificity of the autoantibodies and of the autoreactive T cells was investigated and several autoantigens were proposed, in particular glutamic acid decarboxylase (GAD). This enzyme exists in 2 forms (GAD 65 and **GAD 67**) encoded by 2 independent genes. To explain the role of GAD in type I diabetes, the authors prepd. recombinant rat GAD 65 as fusion protein, produced in an Escherichia coli expression system, and they treated NOD female mice from 4 to 7 wk of age by repeated i.p. injections of 5 .mu.g fusion protein (3 injections per wk); control groups received the fusion partner, maltose binding protein (MBP) or dissolving agent (NaCl 0.9%). The authors investigated 2 parameters, the degree of insulitis 5 wk after the last injection and the overall incidence of the **disease**. Histol. examn. of the pancreata from GAD-treated mice revealed a redn. in the severity of insulitis compared with the 2 control groups. Furthermore, the authors obsd. that the time of onset and the frequency of diabetes in NOD females injected with GAD fusion protein differed from the control groups receiving MBP or NaCl. Thus, a 3-wk treatment of NOD female mice starting at 4 wk of age protects them from diabetes, again emphasizing the crucial role of GAD as autoantigen in type I diabetes.

L21 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:698330 CAPLUS
DOCUMENT NUMBER: 121:298330
TITLE: Diabetes enhancement and increased islet antigen expression following neonatal injections of glucose and arginine in non-obese diabetic mice
AUTHOR(S): Senecat, Odile; Martignat, Lionel; Elmansour, Amina; Charbonnel, Bernard; Sai, Pierre
CORPORATE SOURCE: Sch. Med., Nantes Univ., Nantes, Fr.
SOURCE: Metab., Clin. Exp. (1994), 43(11), 1410-18
CODEN: METAAJ; ISSN: 0026-0495

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Modulation of .beta.-cell antigens at birth may affect the course of type I diabetes. Since the functional state of .beta. cells modulates antigen expression, the authors investigated whether neonatal injections of glucose and arginine (G-A) influence diabetes in non-obese diabetic (NOD) mice. Two groups of 90 mice (45 female, 45 male) were injected for the first 6 days of life with G-A or saline. To det. whether these injections influenced .beta. cell functional maturation, isolated islets were characterized according to insulin response to glucose or arginine. Modulation of antigens for islet-cell autoantibodies (ICA antigens) was analyzed by indirect immunofluorescence using ICA-pos. human sera. Variations of pancreatic glutamic acid decarboxylase 67 kDa (**GAD 67**) mRNA were evald. by polymerase chain reaction (PCR), hybridization with a 32P-labeled probe, and densitometry of the autoradiog. bands. Female NOD mice treated with G-A displayed diabetes earlier and with a higher incidence than control mice, whereas the diabetes incidence was not statistically modified in G-A-treated male NOD mice. Insulitis was more severe in 2-mo-old G-A-treated female NOD mice than in control mice, but was not statistically modified in male NOD mice. In both sexes, ICA antigen and **GAD 67** mRNA were higher in G-A-treated mice than in control mice. Islets isolated after neonatal G-A injections exhibited improved insulin sensitivity to both stimuli. Splenocyte subsets analyzed by cytofluorometry, as well as splenocyte proliferations in the presence of concanavalin or rat insulinoma cells or during syngeneic mixed-lymphocyte reaction, were not modified after G-A treatment. The authors conclude that neonatal injections of G-A enhance diabetes in female NOD mice. Even though hypotheses as to the direct effects on the immune system or deleterious effects of glucose and arginine on the .beta. cells cannot be excluded, the mechanisms behind the clin. effect could be related to accelerated maturation of .beta. cells and overexpression of islet antigens during the completion of immune self-tolerance, or to amplification of the destructive process due to the existence of more targets for effector cells. The same treatment does not significantly affect diabetes in male NOD mice whose resistance to **disease** could not be overcome simply by peripheral modulation of .beta.-cell antigens.

L21 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:624130 CAPLUS
DOCUMENT NUMBER: 119:224130
TITLE: Identification of a dominant epitope of glutamic acid decarboxylase (GAD-65) recognized by autoantibodies in stiff-man syndrome
AUTHOR(S): Butler, Margaret Husta; Solimena, Michele; Dirkx, Ron; Hayday, Adrian; De Camilli, Pietro
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA
SOURCE: J. Exp. Med. (1993), 178(6), 2097-106
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glutamic acid decarboxylase (GAD) is the enzyme that synthesizes the neurotransmitter GABA in neurons and in pancreatic .beta. cells. It is a major target of autoimmunity in stiff-man syndrome (SMS), a rare neurol. **disease**, and in insulin-dependent diabetes mellitus. The two GAD isoforms, GAD-65 and **GAD-67**, are the products of two different genes. **GAD-67** and GAD-65 are very similar to each other in amino acid sequence and differ substantially only at their N-terminal region. The authors have investigated the reactivity of

autoantibodies of [redacted]iff-man syndrome patients to G[redacted] All patient sera contained antibodies that recognize strongly GAD-6[redacted] but also **GAD -67**, when tested by immunopptn. on brain exts. and by immunopptn. or immunocytochem. on cells transfected with either the GAD-65 or the **GAD-67** gene. When tested by Western blotting, all patient sera selectively recognized GAD-65. Western blot anal. of deletion mutants of GAD-65 demonstrated that autoantibodies are directed predominantly against two regions of the GAD-65 mol. All SMS sera strongly recognized a fragment contained between amino acid 475 and the C terminus (amino acid 585). Within this region, amino acids 475-484 and 571-585 are required for reactivity. The requirement of these two discontinuous segments suggests the epitope is influenced by conformation. This reactivity is similar to that displayed by the monoclonal antibody GAD 6, suggesting the presence of a single immunodominant epitope (SMS-E1) in this region of GAD-65. In addn., most SMS sera recognized at least one epitope (SMS-E2) in the N-terminal domain of GAD-65 (amino acids 1-95). The demonstration in SMS patients of a strikingly homogeneous humoral autoimmune response against GAD and the identification of dominant autoreactive target regions may help to elucidate the mol. mechanisms of GAD processing and presentation involved in GAD autoimmunity. Moreover, the reactivity reported here of GAD autoantibodies in SMS partially differs from the reactivity of GAD autoantibodies in insulin-dependent diabetes mellitus, suggesting a link between the pattern of humoral autoimmunity and the clin. condition.

L21 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1993:425825 CAPLUS
DOCUMENT NUMBER: 119:25825
TITLE: Demonstration of GAD-65 as the main immunogenic isoform of glutamate decarboxylase in type 1 diabetes and determination of autoantibodies using a radioligand produced by eukaryotic expression
AUTHOR(S): Velloso, Licio A.; Kaempe, Olle; Hallberg, Anders; Christmanson, Lars; Betsholtz, Christer; Karlsson, F. Anders
CORPORATE SOURCE: Dep. Intern. Med., Univ. Hosp., Uppsala, Swed.
SOURCE: J. Clin. Invest. (1993), 91(5), 2084-90
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasmids contg. cDNA for the rat 67- and 65-kDa isoforms of glutamate decarboxylase (**GAD-67** and GAD-65) were expressed in COS-cells, and lysates of the [35S]methionine-labeled cells were then used for immunopptns. Blood sera from 38 patients with type 1 (insulin-dependent) diabetes mellitus, which pptd. a 64-kD antigen from rat pancreatic islets, reacted with the recombinant GAD-65 in relation to their anti-64-kD titers. The 8 strongest sera also pptd. the recombinant **GAD-67**, suggesting that certain epitopes are common to both isoforms. The [35S]methionine-labeled GAD-65 was purified from COS cell lysates and used in binding assays with 50 sera of patients with recent onset of type 1 diabetes mellitus. 38 Sera (76%) pptd. the labeled GAD-65 with titers that correlated with islet cell antibodies (ICA) detd. in a std. immunofluorescence assay. 2 Sera were GAD pos. but ICA neg., 4 were pos. only for ICA, and 6 were neg. for both GAD and ICA, as were the sera of 20 controls. Thus, antibodies against GAD-65 are present in most patients with type 1 diabetes mellitus and autoantibodies against other islet cell antigens also exist. The radioligand-binding assay for detecting the GAD antibodies may facilitate screening of individuals with autoimmune islet cell **disease**.

L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:382651 CAPLUS
DOCUMENT NUMBER: 131:139817
TITLE: An increase in glutamate release follows a decrease in gamma aminobutyric acid and the pubertal increase in luteinizing hormone releasing hormone release in female rhesus monkeys
AUTHOR(S): Terasawa, E.; Luchansky, L. L.; Kasuya, E.; Nyberg, C. L.
CORPORATE SOURCE: Wisconsin Regional Primate Research Center and Department of Pediatrics, University of Wisconsin, Madison, WI, 53715-1299, USA
SOURCE: J. Neuroendocrinol. (1999), 11(4), 275-282
CODEN: JOUNE2; ISSN: 0953-8194
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previously the authors have shown that release of .gamma.-aminobutyric acid (GABA) in the stalk-median eminence (S-ME) is high in prepubertal monkeys and that a decrease in GABA release triggers the onset of puberty.

However, it is still unclear how disinhibition of the LH releasing hormone (LHRH) neuronal system from GABA input is followed (or accompanied) by an increase in stimulatory signals, such as glutamatergic input to LHRH neurons. To clarify the temporal relationship between the redn. of the GABAergic inhibitory signal and the enhancement of the glutamatergic stimulatory signal in the control of LHRH release at the onset of puberty, the authors conducted two expts. using a push-pull perfusion method. In the first expt., the authors measured developmental changes in release of LHRH, GABA, and glutamate in the S-ME. LHRH levels were very low in prepubertal monkeys, increased to higher levels in early pubertal monkeys, with the highest LHRH levels occurring in mid-pubertal monkeys. As the authors previously obsd., GABA levels were high in prepubertal monkeys and then decreased in early- and mid-pubertal monkeys. In contrast, glutamate levels were very low in prepubertal monkeys, increased dramatically in early pubertal monkeys, and then slightly decreased in mid-pubertal monkeys, although mid-pubertal levels remained much higher than prepubertal levels. In the second expt., the authors measured GABA, glutamate and LHRH in the same samples obtained from prepubertal monkeys which were infused with an **antisense** oligodeoxynucleotide (AS) for glutamic acid decarboxylase (**GAD**) **67** mRNA into the S-ME. GAD67 is a catalytic enzyme for GABA synthesis from glutamate, and AS GAD67 mRNA interferes with GAD67 synthesis. Infusion of the AS GAD67 induced a decrease in GABA release, which subsequently resulted in an increase in LHRH release. Surprisingly, glutamate release also increased several hours after the decrease in GABA release, and the increased LHRH release continued. These data are interpreted to mean that a decrease in GABA synthesis by interference with GAD67 synthesis and the redn. of GABA release in the S-ME trigger an increase in LHRH release, but that a subsequent increase in glutamate release in the S-ME further contributes

to the pubertal i[redacted]ease in LHRH release at the on[redacted] of puberty. The data further support the authors' hypothesis that [redacted] plays an important role in the mechanism of the onset of puberty.

L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:708510 CAPLUS
DOCUMENT NUMBER: 126:5809
TITLE: Glutamate decarboxylase-67 messenger RNA expression in
normal human basal ganglia and in **Parkinson**'s disease
AUTHOR(S): Nisbet, A. P.; Eve, D. J.; Kingsbury, A. E.; Daniel, S. E.; Marsden, C. D.; Lees, A.; Foster, O. J. F.
CORPORATE SOURCE: Parkinson's Disease Society Brain Bank, London, WC1N 1PJ, UK
SOURCE: Neuroscience (Oxford) (1996), 75(2), 389-406
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Expression of glutamate decarboxylase-67 mRNA was examd. in the basal ganglia of normal controls and of cases of **Parkinson**'s disease using in situ hybridization histochem. in human post mortem material. In controls glutamate decarboxylase-67 mRNA expression was detected in all large neurons in both segments of the globus pallidus and in three neuronal subpopulations in the striatum as well as in substantia nigra **reticulata** neurons and in a small sub-population of subthalamic neurons. In **Parkinson**'s disease, there was a statistically significant decrease of 50.7% in glutamate decarboxylase-67 mRNA expression per neuron in the lateral segment of the globus pallidus (controls: mean 72.8 .mu.m2 .+-. S.E.M. 8.7 of silver grain/neuron,; **Parkinson**'s disease: mean 35.9 .mu.m2 .+-. S.E.M. 9.7 of silver grain/neuron, Student's t-test). In the medial segment of the globus pallidus, there was a small, but non-significant decrease of glutamate decarboxylase-67 mRNA expression in **Parkinson**'s disease (controls: mean 100.6 .mu.m2 .+-. S.E.M. 7.2 of silver grain/neuron; **Parkinson**'s disease: mean 84.8 .mu.m2 .+-. S.E.M. 13.0 of silver grain/neuron). No significant differences in glutamate decarboxylase-67 mRNA were detected in striatal neuronal sub-populations between **Parkinson**'s disease cases and controls. These results are the first direct evidence in humans that there is increased inhibitory drive to the lateral segment of the globus pallidus in **Parkinson**'s disease, as suggested by data from animal models. The authors therefore provide theor. support for current exptl. neurosurgical approaches to **Parkinson**'s disease.

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:318547 CAPLUS
DOCUMENT NUMBER: 122:98977
TITLE: Neurotoxic effect of intranigral injection of 1-methyl-4-phenylpyridinium on GABA-containing neurons
and its relation to circling behavior
AUTHOR(S): Jasso-Lopez, Diana; Tapia, Ricardo
CORPORATE SOURCE: Dep. Neurociencias, Univ. Nacional Autonoma Mexico, Mexico City, Mex.
SOURCE: J. Neurochem. (1995), 64(2), 794-801
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ionic species 1-methyl-4-phenylpyridinium (MPP+) seems to be the

metabolite responsible for the damage to dopaminergic neurons occurring after administration of the **parkinsonian** drug 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine. In the present study the authors show that the unilateral stereotaxic microinjection of MPP+ into the substantia nigra pars **reticulata** in rats produces immediately intense and long-lasting (up to 96 h) contralateral turning behavior in a dose-dependent manner. This behavioral effect was correlated with a dose-dependent manner. This behavioral effect was correlated with a dose- and time-dependent decrease (up to 90%) of glutamate decarboxylase activity and with a notable loss of neurons in the injected nigra **reticulata**. GABA levels in the injected nigra were also decreased, whereas the dopamine concn. in the ipsilateral striatum was not affected at 24 h, when maximal behavioral effects were obsd. The circling behavior was presented by the dopamine carrier blocker nomifensine only during the first 2 h, whereas the dopamine receptor antagonist haloperidol was ineffective. The results indicate that MPP+ is toxic for inhibitory GABAergic neurons in the nigra pars **reticulata** and, furthermore, suggest that disruption of the function of these GABAergic neurons may be involved in the abnormal motor behavior produced by the injection of MPP+ in the substantia nigra.

L11 ANSWER 3 OF 3 CAPLUS
ACCESSION NUMBER: 1976:103494 CAPLUS
DOCUMENT NUMBER: 84:103494
TITLE: Distribution of choline acetyltransferase and glutamate decarboxylase within the substantia nigra and in other brain regions from control and **Parkinsonian** patients
AUTHOR(S): Lloyd, K. G.; Moehler, H.; Heitz, Ph.; Bartholini, G.
CORPORATE SOURCE: Dep. Exp. Med., F. Hoffmann-La Roche und Co. Ltd., Basel, Switz.
SOURCE: J. Neurochem. (1975), 25(6), 789-95
CODEN: JONRA9
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Choline acetyltransferase (EC 2.3.1.6) (I) and glutamate decarboxylase (EC 4.1.1.15) (II) activities in the substantia nigra of **Parkinsonian** brains were 15-20% of those in substantia nigra from control brains. In control substantia nigra I activity in the pars compacta was 427 and 253% higher than in the pars **reticulata** and intermediate region resp. and II activity in pars compacta was 41% higher than in pars **reticulata**, whereas in substantia nigra of **Parkinsonian** brains no distinctive distribution of I and II activities was obsd. However, within pars compacta I activity was lower in the medial than in the rostral part. In control brains I activity was highest in the caudate nucleus and putamen and II activity was highest in substantia nigra, caudate nucleus, putamen, and cerebral cortex. In **Parkinsonian** brain the only significant redn. in I and II activities was in the substantia nigra.

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L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
AN 1992:400687 CAPLUS
DN 117:687
TI Effects of chronic levodopa on D1 and D2 receptor-mediated striatal output
AU Engber, T. M.; Susel, Z.; Weick, B. G.; Walters, J. R.; Chase, T. N.
CS Exp. Ther. Branch, NINDS, Bethesda, MD, 20892, USA
SO Neurochem. Int. (1992), 20(Suppl.), 255S-260S
CODEN: NEUIDS; ISSN: 0197-0186
DT Journal
LA English
CC 1-11 (Pharmacology)
AB A series of studies are described on dopaminergic regulation of striatal output conducted in rats with a unilateral 6-hydroxydopamine lesion of the median forebrain bundle treated chronically with the dopamine precursor levodopa. The expts. included behavioral, neurochem., electrophysiol., and glucose utilization expts. The data are consistent with the hypothesis that dopaminergic D1 and D2 receptor-mediated striatal output occurs predominantly by way of anatomically sep. pathways. The effects of D1 receptor stimulation are mediated primarily by striatonigral and striatoentopeduncular neurons, while the effects of D2 receptor stimulation are mediated primarily by striatopallidal neurons. Levodopa appears to decrease the sensitivity of the striatonigral pathway to D1 receptor stimulation and increase the sensitivity of the striatopallidal pathway to D2 receptor stimulation. In addn., chronic levodopa treatment did not alter either D1 or D2 receptor binding in the striatum, but it did alter **glutamic acid decarboxylase** activity, peptide content in striatonigral neurons and the response of cells in the substantia nigra pars **reticulata** to GABA. These findings have implications in the treatment of **Parkinson**'s disease.
ST levodopa striatum neurotransmission dopaminergic receptor
IT Neurotransmission
(in brain striatum, levodopa effect on, dopaminergic D1 and D2 receptors mediation of)
IT Receptors
RL: BIOL (Biological study)
(dopaminergic D1, brain striatum neurotransmission response to levodopa mediation by)
IT Receptors
RL: BIOL (Biological study)
(dopaminergic D2, brain striatum neurotransmission response to levodopa mediation by)
IT Brain
(striatum, neurotransmission by, levodopa effect on, dopaminergic D1 and D2 receptor mediation of)
IT 59-92-7, Levodopa, biological studies
RL: BIOL (Biological study)
(brain striatum neurotransmission response to, D1 and D2 dopaminergic receptor mediation of)